ESTIMATION OF EXPOSURE OF PERSONS IN CALIFORNIA FROM SPECIAL LOCAL NEED USE OF PERMETHRIN ON HUMAN CLOTHING

By

Tareq A. Formoli, Associate Pesticide Review Scientist

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California Environmental Protection Agency
Department of Pesticide Regulation
Worker Health and Safety Branch
1220 N Street
Sacramento, California 95814

ABSTRACT

Permethrin is a contact insecticide which has a wide range of agricultural and non-agricultural uses. A formulated product containing 0.5 percent permethrin has been proposed for Special Local Need use on human clothing to repel and kill ticks, mosquitoes and chiggers as a preventive measure against vectors of Lyme disease. Only 11 illnesses/injuries have been reported during 1984-1988 that were associated with the use of permethrin. Human dermal absorption of permethrin is estimated to be about 2 percent. Absorbed Daily Dosage from dermal and inhalation exposure of a person to the spray and to the clothing sprayed with a 0.5 percent formulation of permethrin is estimated at 4.2 ug/kg/day for an adult human.

This report was prepared as Appendix B to the Department's risk assessment document for permethrin use on human clothing because of possible oncogenic and reproductive adverse effects observed in laboratory mice and rats, respectively.

APPENDIX B

California Department of Food and Agriculture
Worker Health and Safety Branch

Human Exposure Assessment
Permethrin
For Use on Human Clothing

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INTRODUCTION

Permethrin is a synthetic pyrethroid. Its chemical name is (3-phenoxyphenyl) methyl (±) cis, trans -3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylate with various cis-trans isomer mixtures. Permethrin is an odorless, pale yellow liquid or colorless solid. It is almost insoluble in water (<1 ppm), but soluble in most organic solvents. It melts at approximately 35 ^{o}C. Its vapor pressure at 50 ^{o}C is < 1 X 10^{-6} mm Hg. Permethrin is used as a contact and residual insecticide.

EPA STATUS

A number of Special Local Need (SLN) registrations have been granted in several states pursuant to section 24(c) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) for use of permethrin on human clothing. An SLN registration of a 0.5 percent permethrin product "Permanone Tick Repellent" has been requested for use on human clothing in California to repel and kill ticks, mosquitoes and chiggers. The application for registration of this SLN is currently under review in California.

USAGE

Permethrin has a wide range of agricultural and non-agricultural uses. About 181,000 pounds (lbs) of permethrin active ingredient (a.i) were sold in California in 1988 (1). The Annual Use Report indicates that approximately 140,000 lbs of ai were used in California in 1988, almost entirely for agricultural uses including livestock and livestock buildings (2). Only 3 lbs were reported as used for public health pest control. All users are not required to submit use reports for permethrin. This could be the reason for the discrepancy between the amount sold and the amount used in California in 1988. The proposed product for this SLN is currently registered for uses such as control of residential, industrial, garden, pet and livestock insects. It can also be used on premises, bedding, furniture and other infested inanimate objects. The primary purpose of this SLN is to use Permanone Tick Repellent on human clothing as a preventive measure against vectors of Lyme disease. Statements supportive of this SLN indicate the existence of the vectors of Lyme disease in California and the lack of any vaccine against Lyme disease (3, 4). The proposed SLN label instructs the user to spray clothing with a slow sweeping motion using one half content (85 grams) of an entire container. Treatment is to take about two minutes and must be made at least two hours prior to wearing the clothing.

FORMULATION

The product for the proposed SLN is an aerosol 0.5 percent permethrin formulation in pressurized 6-oz containers.

LABEL PRECAUTION

The product for the proposed SLN is a toxicity category III pesticide bearing the signal word "Caution". The label prohibits the use of this product in a manner such that it would come in direct contact with skin, face or eyes. The label instructs the user not to retreat clothing more than once every

two weeks. Clothing must be laundered at least once before retreating. The label does not limit the use of this product to treat one set of clothing once in two weeks. The product label alerts the user to avoid breathing vapors or spray mist. A statement of practical treatment on the label provides instruction in case of accidental exposure.

ILLNESS/INJURY REPORTS

A total of 11 illnesses/injuries (7 systemic and 4 skin) have been reported by physicians in California during 1984-1988 that were associated with exposure to permethrin or permethrin residues (5). These incidents were related to agricultural and non-agricultural uses of permethrin, involving five workers handling the pesticide or contacting pesticide residues, two home-residents, and four emergency response personnel (police and fire fighters). These incidents occurred as the result of permethrin uses that are not similar to the use that is proposed in this SLN. Skin, eye, or inhalation exposures resulted in reports of skin rashes, skin/eye irritation, watery eyes, coughing, laryngitis, headache, dryness of nasal and oral mucous membranes and stomach cramps.

DERMAL TOXICITY

Human skin contact with liquid or volatilized permethrin can induce paresthesia (stinging, burning and tingling, progressing to numbness) that is not allergic in nature (6, 7). Burning and itching felt at the site of application by persons treated with permethrin for louse and flea infestation are said to be mainly caused by the parasites themselves and is not typical of the paresthetic reaction mentioned above(7). A dermal irritation study of the formulated product (0.5% permethrin) has resulted in mild skin irritation in rabbits (8). No skin sensitization was observed in guinea pigs treated with this formulation (9).

DERMAL ABSORPTION

A number of dermal absorption studies of permethrin in human and laboratory animals, in vitro or in vivo, have recently been submitted to the Department. Animal percutaneous absorption studies have shown that dermal absorption varies among species and is generally higher than humans (10, 11, 12, 13). Different formulations of permethrin applied to human skin in vivo or in vitro have shown dermal absorption of generally below 2 percent in 24 hours or longer. However, it has been shown that hair, treated with permethrin creme rinse, retained a significant portion of the applied permethrin, thus contributing to reduced absorption of permethrin when applied to human hair and scalp (14). A human study of permethrin shampoo versus aerosol applied to the hair has revealed that permethrin was absorbed approximately 7 times more when treated as an aerosol compared to a shampoo (15). The absorption rate for either formulation was measured at less than one percent. In an in vitro study, human chest skin exposed to ^{14}C- labelled permethrin for 8 hours had a dermal absorption of 0.62 percent (12).

In a dermal absorption study of permethrin in humans, ^{14}C-permethrin was applied to the shaved back of six volunteers at the rate of 8 ug/cm^2 (2040 ug/256 cm^2) using isopropanol (20 %) as a carrier (16). The treated area was covered with a dressing and washing was avoided for 5 days. The dressing was changed every 24 hours. A part of the treated skin was stripped with 20 pieces of adhesive tape at each dressing change. Plasma at specific times and cumulative urine and feces were obtained continuously and kept frozen until shipped to the laboratory. Plasma radiocarbon levels appeared to peak about 24 hours after the treatment with the highest level measured at 0.31 ng/mL and then rapidly declined. The majority of excreted radiocarbon was found in urine, ranging from 0.29 to 2.00 percent of the applied dose in 5 days. Fecal radiocarbon levels were negligible (<4% of the excreted ^{14}C). After 24 hours of treatment, ^{14}C levels on skin measured by tape stripping averaged 8.1 percent of the applied dose. Skin ^{14}C levels declined each day to mean values of 3.2, 0.6, 0.1 and 0.03 percent of the applied dose for days 2, 3, 4, and 5 after the application, respectively.

Although the absorption rate in the above study (0.29 to 2.00 percent) is from five days of exposure and the absorption rate of the human skin in vitro study (0.62 percent) is from 8 hours of exposure, the confounding effects of hair and cream vehicles have been eliminated in these two studies. Based on

these observations, a dermal absorption of 2 percent will be assumed in calculating Absorbed Daily Dosage (ADD).

HUMAN EXPOSURE

The use directions for this SLN are such that the product is sprayed with a slow sweeping motion to moisten the outer surface of clothing from a distance of 6 to 8 inches before the clothing is worn. The efficacy data suggest a range of 15 to 60 seconds of spraying time with 0.5 percent permethrin for effective control of ticks (17). The amount of permethrin (a.i.) on clothing was estimated in the range of 4 to 12.8 ug/cm^2 (17, 18, 19). However, the product label for this SLN suggests a total of 120 seconds of spraying time, using 85 g of the product. Assuming that 10 percent of this amount disperses in the air, the remaining 76.5 g (382 mg a.i.) of the actual spray (formulated pesticide product) would reach the clothing of 18,000 cm^2 surface area. This is equal to 21.2 ug a.i./cm^2 clothing.

Laundering permethrin impregnated fabrics in a complete wash cycle removed 20 - 33 percent of the permethrin present in the clothing (20). Subsequent laundering removed only an additional 6 percent of permethrin in the second laundering. A steady loss of 2 to 3 percent per wash was observed in the third to tenth laundering. The same study indicated that rabbits wearing contaminated fabrics for seven days absorbed about 1.8 percent of the dose remaining after laundering.

Based on a biweekly retreatment and weekly laundering schedule in a six month period, the average accumulated residues on clothing would be 66.0 ug/cm^2 for the weeks treatments were made and 52.8 ug/cm^2 for the weeks that no treatments were made (Table 1).

Table 1

Permethrin Accumulation
on Treated clothes

Week	Applied (ug/cm^2)	Accumulated (ug/cm^2)	Lost (%)
1st	21.2	21.2	-20
2nd		17.0	-6
3rd	21.2	37.2	-20
4th		9.7	-6
25th	21.2	83.4	-20
26th		66.7	-6

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Residue migration studies of permethrin from treated fabrics to rabbit skin have demonstrated 4.5% or 2.8% migration in the first week or the second week of continuous dermal exposure, respectively (21). The migration was generally higher during the first few days of the week. The migration was calculated at 0.9%/day during the first week and 0.56%/day during the second week. The average amount of accumulated permethrin (a.i.) available for daily dermal absorption could be 0.59 ug/cm^2 in a week that a treatment was made and 0.30 ug/cm^2 in the following week that no treatment was made.

Approximately 18,000 cm^2 of an adult human body surface area can be covered with normal clothing such as long-sleeved shirt and long pants. Consequently, the total amount of permethrin (a.i.) available

for dermal absorption would be 10.7 mg/person/day in a week that a treatment was made and 5.3 mg/person/day in the following week that no treatment was made.

The potential for inhalation exposure occurs during the application (approximately 120 seconds). Assuming that during this period 90 percent of the spray reaches the target (76.5 g) and the remaining 10 percent (8.5 g) disperses in a volume of 2.5 m^3 of the air in the user's breathing zone, approximately 0.5 mg/person/day (7 ug/kg/day) permethrin may be inhaled in 120 seconds of exposure. This estimate is calculated based on the EPA's human breathing rate of 29 liters per minute, and a 50 percent respiration uptake (22, 23). The label instructs users to avoid breathing vapors or mist to reduce the potential for inhalation exposure. This instruction to avoid breathing the mist coupled with an estimate for inhalation rate during light work (actual inhalation rate during spraying is probably closer to rest or less than half of the work rate) causes this estimate to be very conservative. Potential inhalation exposure, if any, during the period that the clothing is worn, is expected to be negligible due to the very low vapor pressure of permethrin.

Fall and winter are reported to be the periods of greatest adult I pacificus tick activity in north coastal California, while deer ticks that also may cause Lyme disease are generally acknowledged to be active from April to October (19, 24). The following scenario was assumed as a logical extreme case that could occur without violating label instructions: Using 5 sets of laundered clothing, a person treats and wears one set of clothing each day for 5 days in the first week. After laundering all 5 sets of worn clothing, the same person wears (no retreatment) one set of laundered clothing each day for 5 days in the next week. This two-week cycle is repeated in a sequence that each set of clothing is retreated only once in two weeks during six months in a year. Calculated Absorbed Daily Dosage (ADD), Annual Average Daily Dosage (AADD), and Lifetime Average Daily Dosage (LADD) for a person spraying and then wearing the clothing as described in the extreme case scenario are shown in Table 2.

Table 2
Estimated Exposure of a Person to Permethrin as a
Result of Its SLN Use on Human Clothing

Week of:	Calculated Exposure Dermal (mg/person/day)	Inhalation (mg/person/day)	ADD[a] (ug/kg/day)	AADD[b] (ug/kg/day)	LADD[c] (ug/kg/day)
Treatment	10.7	1.0	7.3		
No Treatment	5.3	0.0	1.1		
Average	8.0	0.5	4.2	2.1	1.2

a - Assuming dermal absorption of 2 percent, respiration uptake of 50 percent, 5 applications every two weeks, five working days a week, body weight of 70 kg.
b - Six months use season in a year.
c - Forty years of working exposure.

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As it was shown (Snodgrass, 1988), little (2-3 percent in third to tenth laundering) permethrin could be removed in laundry. Thus, it should be noted that it is likely that more leaching would occur under laundering conditions than under the conditions which clothing are worn, resulting in negligible off season exposure.

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